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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/539,451	06/20/2005	Malcolm Francis Graham Stevens	620-368	6809
23117	7590	10/20/2006	EXAMINER	
NIXON & VANDERHYE, PC 901 NORTH GLEBE ROAD, 11TH FLOOR ARLINGTON, VA 22203			KOSACK, JOSEPH R	
			ART UNIT	PAPER NUMBER
			1626	
DATE MAILED: 10/20/2006				

Please find below and/or attached an Office communication concerning this application or proceeding.

<b>Office Action Summary</b>	<b>Application No.</b>		<b>Applicant(s)</b>	
	10/539,451		STEVENS ET AL.	
	<b>Examiner</b>		<b>Art Unit</b>	
	Joseph Kosack		1626	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

#### Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

#### Status

- 1) ☒ Responsive to communication(s) filed on 19 July 2006.
- 2a) ☐ This action is **FINAL**.                      2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

#### Disposition of Claims

- 4) ☒ Claim(s) 90-137 is/are pending in the application.
- 4a) Of the above claim(s) \_\_\_\_\_ is/are withdrawn from consideration.
- 5) ☐ Claim(s) \_\_\_\_\_ is/are allowed.
- 6) ☒ Claim(s) 90-128 and 130-137 is/are rejected.
- 7) ☒ Claim(s) 129 is/are objected to.
- 8) ☐ Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

#### Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on \_\_\_\_\_ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.  
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).  
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

#### Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All    b) ☐ Some \*    c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- \* See the attached detailed Office action for a list of the certified copies not received.

#### Attachment(s)

- |  |   |
|--|---|
| 1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892)            | 4) <input type="checkbox"/> Interview Summary (PTO-413)           |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948)   | Paper No(s)/Mail Date. _____                                      |
| 3) <input checked="" type="checkbox"/> Information Disclosure Statement(s) (PTO/SB/08) | 5) <input type="checkbox"/> Notice of Informal Patent Application |
| Paper No(s)/Mail Date <u>6/20/06, 12/23/05, 7/19/06</u>                                | 6) <input type="checkbox"/> Other: _____                          |

### **DETAILED ACTION**

Claims 90-137 are pending in the instant application.

#### ***Priority***

The claim to priority as a 371 filing of PCT/GB02/05842 filed December 20, 2002 has been acknowledged in the instant application.

#### ***Information Disclosure Statement***

The Information Disclosure Statements filed on June 20, 2005, December 23, 2005, and July 19, 2005 have been considered fully by the Examiner.

#### ***Claim Objections***

Claim 129 objected to as being dependent upon a rejected base claim, but would be allowable if rewritten in independent form including all of the limitations of the base claim and any intervening claims, and for not ending with a period.

#### ***Claim Rejections - 35 USC § 112***

The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 90-128 and 130-137 rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

In the instant application compounds of Formula I and their methods of use are claimed. The threshold for adequate written description for a genus of compounds lies in teaching a representative number of specific compounds within the genus such that a wide range of compounds are presented. The instant application fails to do so since only two examples of the six membered ring are shown within the compounds disclosed within the examples and the substitutions on the indole ring have do not support the wide range that is claimed. The person of ordinary skill, based on the explicit examples presented, would extrapolate the six membered ring to include quinone, cyclohexenone, cyclohexanone, and naphthylquinone, and would limit the indole substitution to hydrogen, fluorine, and methoxy. Therefore, claims 90-128 and 130-137 do not meet the written description provision of 35 U.S.C. 112, first paragraph. This rejection can be overcome by amending the claims such that the claims have firm support within the original disclosure.

Claims 131, 132, and 134-137 rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

Claims 131-137 rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for treating colon, renal, and breast cancer with compounds explicitly shown in the specification, does not reasonably provide enablement for all other cancers and general inhibition of thioredoxin/thioredoxin

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reductase using the various other compounds claimed in claim 90. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make or use the invention commensurate in scope with these claims.

In In re Wands, 8 USPQ2d 1400 (1988), factors to be considered in determining whether a disclosure meets the enablement requirement of 35 U.S.C. § 112, first paragraph, have been described. They are:

1. the nature of the invention,
2. the state of the prior art,
3. the predictability or lack thereof in the art,
4. the amount of direction or guidance present,
5. the presence or absence of working examples,
6. the breadth of the claims,
7. the quantity of experimentation needed, and
8. the level of the skill in the art.

#### The Nature of the Invention

The nature of the invention is the treatment of disorders associated with thioredoxin/thioredoxin reductase along with its inhibition (Claims 134 and 135), which include cancers and related diseases (Claims 131, 132, 136, and 137) and specifically colon and renal cancer (Claim 133).

#### The State of the Prior Art and the Predictability or Lack Thereof in the Art

The state of the prior art is that it involves screening *in vitro* and *in vivo* to determine which compounds exhibit the desired pharmacological activities (i.e. what compounds can treat which specific disease). There is no absolute predictability even in view of the seemingly high level of skill in the art. The existence of these obstacles

establishes that the contemporary knowledge in the art would prevent one of ordinary skill in the art from accepting any therapeutic regimen on its face.

The instant claimed invention is highly unpredictable as discussed below:

It is noted that the pharmaceutical art is unpredictable, requiring each embodiment to be individually assessed for physiological activity. In *re Fisher*, 427 F.2d 833, 166 USPQ 18 (CCPA 1970) indicates that the more unpredictable an area is, the more specific enablement is necessary in order to satisfy the statute. *Berry et al. (J. Med. Chem. 2005, 639-644)* teach the compounds of the claimed invention having activity against breast, colon, and renal cancers, but not any other cancer. See especially Figure 4 on page 642. Assays are provided within the specification for inhibition of thioredoxin/thioredoxin reductase and activity against melanoma and CNS cancer, but since the compounds cited do not have written description as described above, full enablement can not be shown for the claims via the data in the specification.

Hence, in the absence of a showing of correlation between all the diseases claimed as capable of treatment by inhibition of thioredoxin/thioredoxin reductase, one of skill in the art is unable to fully predict possible results from the administration of the compound of claim 1 due to the unpredictability of the role of inhibition of thioredoxin/thioredoxin reductase, and the lack of written description support for the claimed compounds.

*The Amount of Direction or Guidance Present and the Presence or Absence of Working*

*Examples*

As stated above, assays are provided within the specification for inhibition of thioredoxin/thioredoxin reductase and activity against colon cancer, renal cancer, breast cancer, melanoma, and CNS cancer. The specification provides working examples of certain compounds covered by the claims, but not a representative number such that the compounds have written description as described above.

*The Breadth of the Claims*

The breadth of the claims is the treatment of all diseases associated with thioredoxin/thioredoxin reductase along with its inhibition (Claims 134 and 135), which include cancers and related diseases (Claims 131, 132, 136, and 137) and specifically colon and renal cancer (Claim 133).

*The Quantity of Experimentation Needed*

The quantity of experimentation needed is undue experimentation. One of skill in the art would need to determine not only the binding affinity of the instant compounds to thioredoxin/thioredoxin reductase, but the ability of the compounds to treat other cancers and all of the compounds within the claimed invention that have activity.

*The Level of Skill in the Art*

The level of skill in the art is high. However, due to the unpredictability in the pharmaceutical art, it is noted that each embodiment of the invention is required to be individually assessed for physiological activity by in vitro and in vivo screening to

determine which compounds exhibit the desired pharmacological activity and which diseases would benefit from this activity.

Thus, the specification fails to provide sufficient support of the broad use of the compounds of claim 90 for the treatment of diseases mediated by inhibiting thioredoxin/thioredoxin reductase. As a result, necessitating one of skill to perform an exhaustive search for which diseases can be treated by what compounds of claim 90 in order to practice the claimed invention.

Genentech Inc. v. Novo Nordisk A/S (CA FC) 42 USPQ2d 1001 , states that " a patent is not a hunting license. It is not a reward for search, but compensation for its successful conclusion" and "[p]atent protection is granted in return for an enabling disclosure of an invention, not for vague intimations of general ideas that may or may not be workable".

Therefore, in view of the Wands factors and In re Fisher (CCPA 1970) discussed above, to practice the claimed invention herein, a person of skill in the art would have to engage in undue experimentation to test which diseases can be treated by the compound encompassed in the instant claims, with no assurance of success.

This rejection can be overcome deleting the claims.

### ***Conclusion***

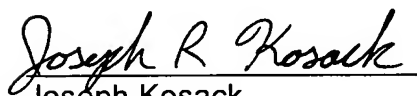
Claims 90-128 and 130-137 are rejected. Claim 129 is objected to. All claims are free of the prior art.

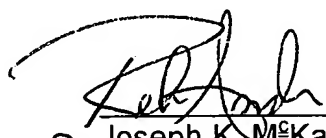


Any inquiry concerning this communication or earlier communications from the examiner should be directed to Joseph Kosack whose telephone number is (571)-272-5575. The examiner can normally be reached on M-F 5:30 A.M. until 2:00 P.M.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Joseph McKane can be reached on (571)-272-0699. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

  
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